

## REMARKS

Claims 1-2, 7 and 10 stand rejected under 35 USC 103(a) as unpatentable over US 20020009426 ('426) in view of WO 2004060965 (WO '965). The Examiner contends that it would have been obvious to one of skill in the art to combine the maleimide linkages of the WO '965 disclosure with the structure of the '426 disclosure to suggest the presently claimed structure.

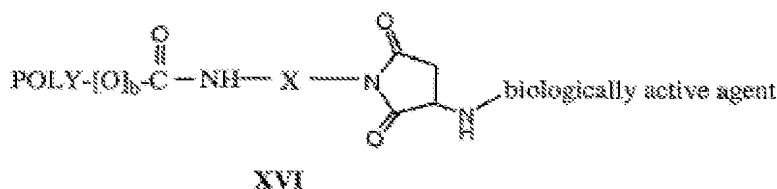
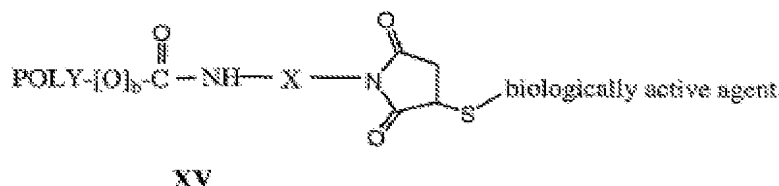
Without acquiescing in the rejection, and solely to advance the prosecution of this application, claim 1 is amended herein without prejudice to be substantially identical to the elected species. In particular,  $V^1$ ,  $V^2$ ,  $B^1$ ,  $B^2$ ,  $Y^1$  and  $Y^2$  are each selected so that there is no additional nitrogen atom between  $X^1$ ,  $X^2$  and the corresponding maleimide moiety, and  $A^1$ ,  $A^2$ ,  $W^1$ , and  $W^2$  are each selected so that the structure between  $X^1$ ,  $X^2$  and the corresponding PEG moiety is NHCO-alkylene. These limitations distinguish the presently claimed structure from the structures disclosed in each of the cited references. In particular, in structures XV and XVII of the WO '965 disclosure cited at page 6 of the office action, the PEG moiety is attached to O-CONH-(alk). Claim 1 is amended herein so that moieties  $A^1$  and  $A^2$  can only be NHCO; the structure CONH has been deleted from  $A^1$  and  $A^2$ , such that claim 1 does not read on the cited structures. For completeness of the record, applicant wishes to point out to the examiner that the first three PEG – maleimide linkages disclosed at page 71 of WO '965 include NHCO, however these structures do not include other elements of the structure recited in claim 1. Thus, even if it were obvious to combine the maleimide linkages of the WO '965 disclosure with the structure of the '426 disclosure, such a combination would not suggest the presently claimed structure.

Claim 1 is further amended to recite the linkers  $L^1$  and  $L^2$  as maleimide residues, each of which is covalently linked to  $Z^1$  and  $Z^2$ , respectively, and each of which is covalently linked through the maleimide nitrogen atom to  $Y^1$  and  $Y^2$ , respectively. This amendment finds support in the specification at page 6, lines 23-26, which states,

“The spacer groups  $L^1$ ,  $L^2$  and  $L^3$  will suitably comprise any moiety familiar to the person skilled in the art which is capable of forming a bridge between the alkylene chain  $Y^1$ ,  $Y^2$  and (where present)  $Y^3$  and the residue  $Z^1$ ,  $Z^2$  and (where present)  $Z^3$  respectively. For example, where  $Z^1$  and/or  $Z^2$  and/or  $Z^3$  is the residue of a polypeptide molecule (e.g. an antibody or a fragment thereof) containing a cysteine residue the corresponding spacer group  $L^1$  and/or  $L^2$  and/or  $L^3$  will suitably be a *maleimide residue*, which may be covalently linked to the cysteine-containing

polypeptide residue  $Z^1$  and/or  $Z^2$  and/or  $Z^3$  via a thiol linkage and to the alkylene chain  $Y^1$  and/or  $Y^2$  and/or  $Y^3$  through the maleimide nitrogen atom.”

(Emphasis added.) This amendment is made because the applicant believes that in the context of the present claims, the term “maleimide residue” is more accurate than the term “maleimide moiety” to describe the structure of the maleimide molecule after it reacts to become bonded to the scaffold structure of the present invention and to an antibody or antibody fragment. At the time the present application was filed, it was well known in the art how maleimide moieties (such as in structure III of the present application) react when used as linker groups. For example, the cited reference WO 2004/060965 at page 16, lines 6-26 illustrates structures XV and XVI wherein a maleimide group is used to link a biologically active agent to a structure:



It may be seen that once the maleimide is linked to both the scaffold and the biologically active agent, it is no longer a true “maleimide moiety,” but is the residue of such a moiety. It is respectfully submitted that the amended claim language is sufficiently supported in the specification, and is sufficiently clear so as to apprise one of skill in the art what the inventor considers to be the invention

In view of the foregoing, the applicants respectfully submit that the term “maleimide residue” is more accurate and its meaning and scope would be understood by those of ordinary skill in the art. As such, this amended claim language meets the requirements of 35 U.S.C. §112.

Claims 6 and 7, which depend from claim 1, are cancelled herein as being merely duplicative in view of the amendments to claim 1. Claim 8 is amended to delete a species no longer encompassed within claim 1 as amended.

It is respectfully requested that further consideration be given to previously withdrawn claims 3 and 9. Claim 3 is amended herein to correspond to amended claim 1, the only difference being that the biologically active moieties Z present in claim 1 are absent in claim 3. Further, claim 3 is amended by substituting structure III for structure II and by deleting the recitation of the L linkers in the text of the claim. The structure III of claim 3 is identical to the structure I of claim 1 as presently amended, except that structure III does not include the biologically active moieties. In other words, structure III is the precursor to structure I. The restriction requirement of January 8, 2008 required the applicants to elect a species of structure I, but was silent as to structure III. It is respectfully submitted that, as claim 1 has already been searched, no additional searching is necessary to examine the structure of claim 3, where the only difference between the subject matter of claim 1 and the subject matter of claim 3 is the absence of the biological moieties. It is therefore proper to rejoin claim 3 and the claims dependent thereon at this time. Claim 4 is the embodiment of claim 3 wherein the linkages to the biologically active moieties are maleimide. As this limitation is now encompassed in amended claim 3, claim 4 is cancelled herein. Claim 9 is amended herein to delete the structure that is no longer encompassed within amended claim 3. It is respectfully submitted that claims 3 and 9 are in condition for allowance.

### **CONCLUSION**

Applicants respectfully submit that the present application is in condition for allowance. Favorable consideration and a notice of allowance of claims 1-3 and 8-10 are respectfully requested.

Respectfully submitted,

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